UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/005,642 | 12/05/2001 | Stephen T. Sonis | 50047/009002 | 8240 |

21559 7590 09/02/2005

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

| EXAMINER | |
|---|---|
| WANG, SHENGJUN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/005,642 | SONIS, STEPHEN T. | |
| | Examiner | Art Unit | |
| | Shengjun Wang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5 and 6* is/are pending in the application.

4a) Of the above claim(s) *2 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



S.D

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on May 9, 2005 has been entered.

### *Claim Rejections 35 U.S.C. 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 3, 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis et al. (USPN 5,654,312) in view of Quinn et al.

3. Andrulis et al. (USPN 5,654,312) teaches that TNF alpha antagonists (such as PTX) and dexamethasone (glucocorticoid/corticosteroid) are useful in treating dermatoses with an autoimmune or inflammatory basis, aphthae is one of the symptoms being effectively treated. see col. 3, line 62 to col. 4, line 55, and the claims in particular. Andrulis particularly teaches the combination of these agents with other anti-inflammatory or other anti autoimmune agents, such as dexamethasone (column 4, lines 38-55). Andrulis teaches topically applied corticosteroids are useful in treating dermatoses with an autoimmune or inflammatory basis, see col. 8, lines 13-40.

Andrulis further teaches that medicaments may be applied to the effected site topically in ointment form, see col. 4, lines 56-60, col. 8, lines 13-40.

4. Andrulis et al. (USPN 5,654,312) does not particularly teach a method of treating oral ulcerations or aphthae by using the particular combination herein.

However, Quirm et al. teaches that aphthae is cause by an underline autoimmune mechanism, see page 4.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the particular TNF antagonist and steroids herein in the treatment of aphthae in general.

One of ordinary skill in the art would have been motivated to employ the combination of TNF antagonists and steroids herein in the treatment of aphthae because both TNF antagonist and steroids are known to be useful in treating dermatoses with an autoimmune or inflammatory basis (e.g., oral aphthae), and each of the agents herein employed are known to be useful for such treatment. Further, Andrulis teaches the benefit for combining different agents. It is also noted that it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two agents known to be useful for treating dermatoses with an autoimmune or inflammatory basis sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

5. Claims 1, 3, 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis et al. (USPN 5,654,312) in view of The Merck Manual (pages 2476-2477), and Ron et al. (US 6,204,270).

6. Andrulis et al. (USPN 5,654,312) teaches that TNF alpha antagonists (such as PTX) and dexamethasone (glucocorticoid/corticosteroid) are useful in treating dermatoses with an autoimmune or inflammatory basis, aphthae is one of the symptoms being effectively treated. see col. 3, line 62 to col. 4, line 55, and the claims in particular. Andrulis particularly teaches the combination of these agents with other anti-inflammatory or other anti autoimmune agents, such as dexamethasone (column 4, lines 38-55). Andrulis teaches topically applied corticosteroids are useful in treating dermatoses with an autoimmune or inflammatory basis, see col. 8, lines 13-40. Andrulis further teaches that medicaments may be applied to the effected site topically in ointment form, see col. 4, lines 56-60, col. 8, lines 13-40.

7. Andrulis et al. (USPN 5,654,312) does not particularly teach a method of treating oral ulcerations or aphthae by using the particular combination herein.

However, The Merck Manual discloses that dexamethasone is particularly known to be useful for treating aphthous topically. See, pages 2476-2477. Ron et al. teaches that PTX, as INF-alpha inhibitor is particularly useful for treating aphthous ulcer in topical dosage form. See, particularly, column 3, lines 36-48, column 4, lines 31-34, and the claims.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the particular TNF-alpha inhibitor (pentoxifylline) and steroid (dexamethasone) herein in the treatment of aphthae in general.

One of ordinary skill in the art would have been motivated to employ the combination of TNF antagonists and steroids herein in the treatment of aphthae because both TNF antagonist and steroids are known to be useful in treating dermatoses with an autoimmune or inflammatory basis (e.g., oral aphthae), and each of the agents herein employed are known to be useful for such treatment. Further, Andrulis teaches the benefit for combining different agents. It is also noted that it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two agents known to be useful for treating dermatoses with an autoimmune or inflammatory basis sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

***Response to the Arguments***

Applicants' amendemnts and remarks submitted May 9, 2005 have been fully considered, but are found unpersuasive.

Applicants contend that Andrulis fails to teach or suggest a composition containing pentoxifylline in the absent of thalidomide for treating aphthous. The arguments are unpersuasive. Note Andrulis teaches the usefulness of TNF-alpha inhibitors in treating dermatoses with an autoimmune or inflammatory basis. Andrulis does not limit the teaching to thalidomide only. Applicants' attention is directed to column 5, lines 40-44, 57-60 and claims 10-12 in Andrulis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617